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10 MAR 1898

BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL.

Vol. IX.—No. 84.] BALTIMORE, MARCH, 1898. [Price, 15 Cents.

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LEPROSY IN THE UNITED STATES, WITH THE REPORT OF A CASE.

By William Osler, M. D., *Professor of Medicine in the Johns Hopkins University.*

[*Clinical Lecture delivered at the Johns Hopkins Hospital, Wednesday, Feb.* 2, 1898.]

To no disease perhaps has attention been more actively called of late years than to leprosy, one of the oldest and most dreaded scourges of the race. In great part this has been due to the activity in England of a Leprosy Commission, and to the establishment of a National Leprosy Fund. Through the energy of Dr. Lassar a Leprosy Conference has recently been held in Berlin, two volumes of the proceedings of which I pass about for your inspection. They contain an immense amount of valuable information with reference to the present status of the disease throughout the world, and the best means for its prevention.

I take this opportunity of again showing to you the case which has been in Ward I for some months, and of speaking upon the present condition of the disease in the United States and the prospects of its spreading. First let me refresh your memories about the patient before you. Her history is as follows: She is now 30 years old. She was born in Baltimore, of French-German parents; her father was a native Frenchman who came here when young; he served in the army, was a very healthy man and had no skin eruption. He died at the age of 50. Her mother, who died at the age of 40, appears to have been a healthy woman. When 16 years old the patient visited an uncle in Demerara, remaining only a few months. This uncle, a native American, is at present in Baltimore, and neither he nor any member of his family has ever had a serious skin disease. On returning to this country she lived in Baltimore, one year in Norfolk, and for the last five years in Alleghany City, Pa. She returned to this city in April, and was admitted to the hospital as a case of obstinate lues.

Her personal history is as follows. She was healthy as a young girl; she married when 20 years old, had one child at 23, which died shortly after birth; she has had one miscarriage since. Her present illness began six years ago. Here is a photograph taken two years prior to the onset of the trouble, from which you can judge of the terrible changes the disease has wrought. She noticed first two brown spots over the elbow, and then several spots on the wrist. She was pregnant at the time, and had with their appearance a little fever and slight indisposition. These spots remained stationary until after her confinement, when they increased in size and became nodular. The disease spread rapidly, the feet being attacked next, beginning on the ankles nearly five years ago. Ever

since there has been a steady appearance of lumps and nodules on the skin of the face, legs and arms. Only during the past year have they appeared above the elbows. Two years ago she lost the eyebrows and lashes; the hair of the head is not falling out. The voice began to get hoarse a few months ago, and eight months since she noticed the formation of scabs in the nose.

Her condition at present is very characteristic of tubercular leprosy. She looks a great deal older than her age; the swollen appearance of the eyebrows and cheeks, the rounded outlines of the nose and of the ears, the absence of eyelashes, and the brownish pigmented discoloration, give a picture that is perfectly characteristic. The neck is only slightly involved, showing only a few pigmented areas. The hands, feet and legs are very much involved, the hands showing scars of erosion and ulceration; the finger-nails are not attacked, but in the left hand are fresh punched-out ulcers. On the arms are scars of several very deep ulcers. On the upper arm the earlier stages are shown, the brownish discoloration, and the skin looks raised and infiltrated, and on palpation one can feel that beneath the skin there is a nodular infiltration. The forehead shows a uniform infiltration. She has little or no disturbance of sensation; she feels touch everywhere and feels pain.

She has been under our care since April last, and has improved in very many ways. The general nutrition is much better. The open ulcers and sores which were present on admission have, as you see, almost entirely healed. During the months of June, July and August she had a great deal of fever, but now for some time the temperature has been normal. She has gained in weight, and is in every way very much more comfortable. She is a very tidy, neat woman, and now is able to look after her own room. I may add that it has been to both physicians and nurses of our staff a great pleasure to be able to care for her and make her comfortable.

Where did this patient contract leprosy? You noticed in the history that she had resided in Demerara in the West Indies, a colony much afflicted with the disease. True, it is now fifteen years since she left there, and it was eight years before the first appearance of the disease. It is well known that the period of incubation may be very much longer, even as long as twenty or thirty years. It may be said that without exception all cases of leprosy met with in the Eastern States are persons who have lived for a shorter or a longer time in countries where the disease prevails. The experience in Great Britain is very instructive in this respect. Abraham estimates that within the past ten years the number of cases has been about one hundred, and so far as is known there has been but one instance in which the disease has been transmitted. This was the well known case reported by Benson, of an Irish soldier who returned from India with leprosy. His brother slept in the same bed with him for at least a year and a half, and after his death he wore the leper's clothes. Three years later the brother became leprous.

You will find in these volumes of the Transactions of the Leprosy Conference—of which by the way there is a very good abstract in Nos. 2 and 4 of the Philadelphia Medical Journal by Dr. Nuttall—a very full discussion of all the problems relating to the disease. Of these by far the most important relates to the method of infection, whether by inoculation, contagion, or hereditary transmission.

The possibility of successful inoculation must be recognized, though Hansen, the leading living expert on leprosy, declares that as yet all attempts at reproducing the disease by direct inoculation have been unsuccessful. He does not regard Arning's experiment on the Honolulu convict as satisfactory, since this man had leprous relatives. A number of observers, including some of the best students of the disease, have inoculated themselves with negative results. The direct hereditary transmission must be excessively rare, more so indeed than in tuberculosis. As lepers have, as a rule, very few children, heredity can only play a very small part in the spread of the disease. Alverez stated at the recent Congress that he had never seen a new-born leper child; the youngest patient he had met with was three and a half years old.

The highly contagious character of leprosy has been a fixed belief for centuries, and much of the popular dread is based upon the highly colored views as to the extreme risk of contact with the disease. For a full discussion of the question I must refer you to the Proceedings of the recent Congress. The opinion was universally in favor of its contagious nature, though the greatest difference of opinion existed as to the methods by which the disease is conveyed, and on this question we really need much more information. An important point was brought out at the Congress as to the much more widespread distribution of the lepra bacilli, particularly in the secretions. In modern times one of the strongest points in favor of the contagious nature of the disease is the manner in which it has spread in the Sandwich Islands. Europeans residing in leprous regions occasionally contract the disease, and with scarcely an exception, as in the patient I have just shown you, cases occurring in leprosy-free regions have a history of a residence for a longer or shorter time in localities in which the disease prevails. On the other hand there are a great many facts which would indicate that it is very difficult to catch the disease. It is true that Father Damien at the leper settlement at Molokai, and Father Boglioli (whose portrait I here show you) in New Orleans, contracted the disease in the discharge of their ministerial duties, but it has been the almost universal experience in the leper settlements and lazarettos that the nurses, physicians and attendants are not attacked. At the Tracadie settlement, which I visited a few years ago, the head Sister told me that during the forty years no Sister or servant had contracted the disease, though the accommodations are rather contracted. Not one of the Sisters who have nursed in the Trinidad Asylum, for now nearly thirty years, has contracted the disease.

A very important question is whether there is any possibility that leprosy will again spread in the more civilized districts of the earth. A good deal of uneasiness has been fostered by sensational newspaper reports. The practical question for us here is, is leprosy spreading in the United States? I have here letters from most of the infected districts, the contents of which I will briefly summarize. Including the two districts in the Dominion of Canada, there may be said to be five foci in which the disease at present prevails.

In the northern part of New Brunswick leprosy has existed in a couple of counties since the early part of the century. The cases as recognized are segregated in the lazarette at Tracadie. Dr. Smith, the physician in charge, writes under date of January 17, 1898: "The number at present in the hospital is twenty-four, eighteen males and six females. . . . Of the above number three are Icelanders whom I brought from Manitoba. Leprosy in Cape Breton has almost died out. With us in New Brunswick segregation is stamping out the disease. The cases have dwindled from about forty in the early history of the disease to about half that number. One of our inmates is a negro I brought recently from St. John, N. B. He had strayed from Bermuda. Leprosy is not on the increase in Canada." In British Columbia the disease has been introduced by the Chinese, but I have recently heard from Dr. Hannington, of Victoria, that there are only eight cases at present in the settlement on Darcy Island. Dr. Hannington does not think that the disease is spreading. Among the Icelandic immigrants in Manitoba there are a few cases, but the strong probability is that it will gradually die out.

In the United States there are three important centres. To "New Scandinavia," as parts of Minnesota and Wisconsin have been called, the disease was introduced by the immigrant Swedes and Norwegians. Altogether more than 150 cases were known. The disease has not spread, and Dr. Bracken, the Secretary of the State Board of Health, wrote January 19, 1898, that there are in Minnesota, so far as is known, only twenty-seven cases, and some of these have probably died since the last return. All of them contracted the disease before coming to America. A very encouraging fact is that no instance of leprosy has been known to be contracted from any of these Norwegian settlers. In California leprosy has been introduced by the Chinese, and in a few instances by native Americans returning with the disease from the Sandwich Islands. The total number of cases, however, is not large, certainly not more than a dozen, and the likelihood of the disease progressing in the native American population is very slight.

By far the most extensive focus of leprosy is in Louisiana. Dr. Isadore Dyer, who was the delegate from Louisiana to the Leprosy Conference in Berlin, has reported fully on the history of the disease in that State, where it has been known since 1785. Dr. Dyer writes under date of January 12, 1898: "My paper on endemic leprosy in Louisiana, read before the Lepra Conference in Berlin, has not yet been published. It is to appear in the third or fourth volume of the Transactions of this meeting. Full tables are given of all recorded leprosy in Louisiana since 1785, the existing acknowledged cases being separately tabulated. This last table contains 118 cases, in addition to which I have seen six within the past four months, making a total of 124 positive living cases to-day." Dr. Dyer thinks that this does not represent by any means all the cases, but says he believes it is quite justifiable to calculate the number of lepers in this State as not less than 300.

A few cases of leprosy are met with in Florida, South Carolina and in others of the Southern States. Now and again cases occur in the eastern cities, invariably imported, as in the patient at present in the hospital. So far as we know, with the exception of the single case recorded by Dr. I. E. Atkinson of this city, there has not been an instance in which the disease has been transmitted from one of these imported cases to a native American.

I believe the danger of the disease spreading and becoming in any way a serious menace to the country is entirely fanciful. In the question of the annexation of Hawaii the danger of leprosy has also come up. This really would not be a serious objection. I have seen a letter from Dr. Day, from Honolulu, in which he claims that the disease is progressively diminishing, and that the statement made by Dr. Prince A. Morrow, of New York, that every one in ten individuals in the Sandwich Islands is leprous is entirely unwarranted. He quotes figures to show that the number of cases segregated in Molokai has progressively diminished in the past few years. In a recent letter to the San Francisco *Chronicle* the President of the Board of Health states that barely one per cent of the population of the Sandwich Islands has leprosy.

The means for combating the existing cases of the disease are perfectly plain and well understood. The Norwegian method of segregation should be enforced in Louisiana and in the State of California. Remarkable results have followed this plan in Norway. In 1856 there were nearly 3000 lepers in Norway; now there are not more than 700, and most of them are in asylums. The segregation should be compulsory in all instances except when the friends can show that they have ample provision in their own home for the complete separation and proper care of the patient.

In the case of the patient you have just seen, as her husband is not in a position to look after her, it is the duty of the city to care for her in a proper way. She should be removed to Bay View, where a room should be provided with a separate arrangement for washing the clothes and disinfecting the body linen. From a humanitarian standpoint we have been very glad to care for her and to do what we could to check the disease in its active and progressive state. Now that she has improved so much I feel that we are no longer bound to keep her, and as she is a free agent, I shall take an early opportunity to discharge her from my care.

NOTICE.

All inquiries concerning the admission of free, part pay, or private patients to the Johns Hopkins Hospital should be addressed to Dr. Henry M. Hurd, the Superintendent, at the Hospital.

Letters of inquiry can be sent, which will receive prompt answer, or personal interviews may be held.

Under the directions of the founder of the Hospital the free beds are reserved for the sick poor of Baltimore and its suburbs and for accident cases from Baltimore and the State of Maryland. To other indigent patients a uniform rate of $5.00 per week has been established. The Superintendent has authority to modify these terms to meet the necessity of urgent cases.

The Hospital is designed for cases of acute disease. Cases of chronic disease are not admitted except temporarily. Private patients can be received irrespective of residence. The rates in the private wards are governed by the locality of rooms and range from $20.00 to $35.00 per week. The extras are laundry expenses, massage, the services of an exclusive nurse, the services of a throat, eye, ear and skin or nervous specialist, and surgical fees. Wherever room exists in the private wards and the condition of the patient does not forbid it, companions can be accommodated at the rate of $15.00 per week.

One week's board is payable when a patient is admitted.

SECONDARY MELANO-SARCOMA OF THE LIVER FOLLOWING SARCOMA OF THE EYE.

By Louis Philip Hamburger, M. D., *Resident Medical Officer, The Johns Hopkins Hospital.*

In an article written in 1889 Litten called attention to the inadequacy of the accounts of melano-sarcoma of the liver following a primary growth in the eye. With the exception of Virchow's classical work on tumors, the condition had not been presented in the text-books of medicine or of pathological anatomy in a manner befitting its importance, and Litten writes, "Even the best special works on diseases of the liver, in German, French, and English, scarcely mention it."

Litten's case was that of a man aged 34 years, whom he saw in November, 1884, with a tumor of the liver. He did not see him again until March, 1888. The man was then cachectic, the tumor had increased in size, and in some places showed fluctuation. The possibility of echinococcus cysts was discussed and one of the fluctuating points was aspirated. A black fluid was withdrawn containing polymorphonuclear cells filled with pigment and many pigmented polygonal cells—the pigment being dark brown and even black in some cells—and finally, a few red blood corpuscles. The patient wore a glass eye, and upon referring to the ophthalmological records it was discovered that the right eye had been removed in January, 1884, for a melanotic sarcoma of the choroid. Thereupon the urine was carefully examined and melanuria was demonstrated. The history of a choroidal tumor, an enlarged and nodular liver and melanuria rendered the diagnosis clear; it was subsequently confirmed at the autopsy.

Since the publication of the above-mentioned paper many cases of liver metastasis following primary melanotic tumor of the eye have been reported, but even now the clinical picture has not received the attention which it deserves. Within a year two patients have presented themselves at the Johns Hopkins Hospital with this condition.

Case I. C. B., male, white, age 42; admitted August 21, 1896, complaining of pain in right side.

Family history unimportant. Patient has never had any serious illness. Five years ago, upon the day he sailed from England to this country, his right eye without apparent cause became inflamed. He received no medical attention and at the end of the voyage the eye was quite blind.

His present illness began six weeks ago with a stabbing pain in right side. He then for the first time noted a small lump over the lower ribs on the right side, which was so painful upon any exertion that he gave up work.

There is anorexia; no vomiting; bowels irregular; he has lost 35 pounds in weight since onset.

Physical Examination. Patient is sparely nourished and rather pale. Right eye atrophied; on seventh rib just outside the right mammillary line there is a hard fusiform enlargement 6½x4 cm. and about 1 cm. in depth. It is firm and seems attached to the rib; the overlying skin is not discolored. Examination of heart and lungs negative.

Abdomen. With the exception of a slight bulging in the right hypochondrium, the abdomen looks natural. Liver flatness begins at the sixth rib in right mammillary line; its edge is palpable 10 cm. below the costal margin; it is less distinctly felt as one reaches the median line. Surface is smooth and firm; edge a little irregular. In the epigastrium are four small flattened prominences which feel like subcutaneus fibro-cartilaginous nodules. Spleen not palpable; no general glandular enlargement. Rectal examination negative. Urine, light amber, acid; specific gravity 1020–26; no albumin or sugar; diazo-reaction present.

September 4th, Dr. Mills removed the atrophied globe, and at its posterior portion a small melano-sarcoma, evidently arising from the choroid, was discovered. The patient remained in the hospital a month. Subsequently, on October 8, 1896, he was readmitted, looking paler and more emaciated, and complaining of pain in right and left sides, epigastrium, right shoulder.

The lower right chest is bulging; abdomen is markedly distended, especially in right hypochondrium. On palpation the edge of the liver is felt about 14 cm. below costal margin in right mammillary line; in right and left hypochondrium the edge feels sharp and normal, but below and to the right it is very hard and nodular. Surface is slightly irregular. The patient remained under observation two weeks, and at his own request was discharged; his subsequent history is not known. During these weeks the liver rapidly increased in size; a small swelling similar to the one on the seventh rib, but about one-third its size, appeared on the fifth rib, right side, at junction of its osseous and cartilaginous portions; lymphatic glands became palpable in right inguinal and left posterior cervical regions.

The second case we were able to study more thoroughly.

Case II. P. W., male, white, age 38 years, admitted July 26, 1897, complaining of pain in the lateral regions of abdomen and in the back on right side. Family history unimportant. Patient has had smallpox and rheumatism, otherwise always healthy. About December, 1890, he was struck in the right eye by the branch of a tree. At the time he paid little attention to the incident, but in the course of the winter the eye began to give him pain and his head ached a great deal. During 1891 his vision began to fail, and in January, 1892, a physician whom he consulted enucleated the eyeball.

Present Illness. Began between two and three years ago, that is, about three years after the enucleation, with pain in the abdomen. For the past year has not been able to do much work, for the pain, which extends all over the abdomen and is of a "burning" character, is rendered more severe by any exertion. During last six months little nodules have appeared over the chest. Does not think complexion is darker than formerly; no jaundice; appetite variable; vomited once last week; three years ago weighed 185 pounds, now 117 pounds; has grown weak. At present he has a great deal of frontal headache. He has had cough for three or four days; slight whitish expectoration.

Physical Examination. Patient is an emaciated man; swarthy complexion; lips and mucous membranes of fair color. He wears a glass eye in the right orbit, and when it is removed a moist glistening brown mass is visible in the posterior portion of orbital cavity. Scattered over arms, thorax, abdomen and back are nodules varying in size from one-half to three and a half cm. in diameter, bluish-green in color, and not adherent to the skin or deep tissues. Percussion note over front of chest resonant. In the supra-clavicular fossæ expiration is prolonged, elsewhere of normal relative length. Percussion note over right half of back below middle of scapula lacks resonance; in this area many medium-sized râles are heard; a few over base of left lung. Elsewhere the lung is clear on percussion and auscultation. Heart sounds feeble but free from murmurs.

Abdomen. Full; costal grooves obliterated. Right costal margin considerably more prominent than left; right half of abdomen is more distended than left; veins are prominent over its surface.

Respiratory movements slight. On deep inspiration a large mass descends in the right half of abdomen. Hepatic flatness begins at the sixth rib in the right mammillary line and extends 5½ cm. below costal margin and 13½ cm. below ensiform cartilage in the median line. On palpation a large firm mass occupies an area the limits of which correspond to those obtained on percussion. The mass (evidently the enlarged liver) is extremely firm and distinctly nodular; its edge is rounded. There is general tenderness over abdomen. Spleen not palpable. No general glandular enlargement. Rectal examination negative; urine showed reactions of melanuria. One of the subcutaneous tumors was removed and proved to be a spindle-cell sarcoma with brown pigment within the cells as well as about them; there was some alveolar arrangement.

Blood. Red blood corpuscles 4,480,000; white blood corpuscles 10,300; hæmoglobin 40 per cent. Differential count: Polymorphonuclears 71.6 per cent.; small mononuclears 17.4 per cent.; large mononuclears 9 per cent.; eosinophiles 2.8 per cent.

After admission the patient had attacks of vomiting and diarrhœa, occasional elevations of temperature, now and then paroxysms of coughing during which he expectorated frothy blood-stained sputa. The abdominal tumor and the growth in the orbit rapidly increased in size, new subcutaneous nodules appeared here and there, he suffered great pain in the abdomen, especially on defecation, became progressively weaker and more emaciated, and finally died on October 13, 1897.

Autopsy. The autopsy, performed by Dr. Flexner, showed the most extensive metastases involving the liver, kidneys, lungs, pancreas, thyroid gland, stomach, intestine, gall-bladder, the abdominal, mediastinal and thoracic lymph glands. The right optic nerve showed a grey degeneration and was atrophied; the meninges were œdematous.

The first case is evidently one of primary sarcoma of the choroid with liver metastases; the second, one of general dissemination following what was presumably a melano-sarcoma of the uveal tract, although an account of the condition of the eye at the time of enucleation could not be obtained.

In each case the loss of an eye, the subcutaneous tumors and enlarged liver contributed to form the characteristic picture of melano-sarcoma; indeed, in the second patient the loss of an eye, the pigmented nodules and the colossal nodular liver descending visibly with each inspiration, enabled one to make the diagnosis *de visu*. In addition to emphasizing the clinical aspect of this condition, the cases serve to illustrate many features of pigmented sarcoma of the eye and its sequelæ.

Following the classification of Virchow, pigmented sarcomata of the eye are divided into three classes: 1. Primary external melano-sarcomata which arise at the scleral border. 2. An orbital variety, springing most probably from the adipose tissue of the orbit. 3. Primary internal melano-sarcomata. It is to this division that the first and probably the second of the present series belong. These are the sarcomata arising from the uveal tract; the great majority have their point of origin in the choroid, and as in our case most frequently from its posterior portion. They are composed of spindle cells, or they may contain besides spindle, round and stellate cells.

The disease is not a common one. With the exception of early childhood, it occurs at all ages. Most of the patients are between forty and sixty years of age; a case has been observed as late as the 84th year.

In each of the above histories one's attention is attracted to certain incidents preceding the development of the tumor. It will be recalled that in the one case there is an account of a trauma one year preceding removal of the globe, and in the other, of an inflammatory trouble coming on five years before the new growth was detected, which had caused meanwhile an atrophy of the eyeball. Now, the association of simple inflammatory conditions, with or without antecedent trauma, and the development of melanotic sarcoma of the eye, has often been commented upon and is frequently so striking that it cannot be dismissed as a chance coincidence. Virchow quotes a number of examples. Thus, Rosas reports the case of a woman who lost her sight through an injury received four years previously while splitting wood. Cooper narrates the case of a woman whose cornea had been cloudy two years as the result of an inflammation. Bowman and Mackenzie each gives an example of the growth developing in an eye in which there was present a condition quite similar to that found in our first patient, namely, *atrophia bulbi*. Particularly instructive is a case reported by Raab, inasmuch as imbedded in the tumor could still be demonstrated a portion of the splinter of wood which a year previously had caused the trauma. In 103 cases Lawford and Collins obtained the history of injury in 6.79 per cent.

Perhaps no other ætiological factors in the domain of new growths have been more discussed than those we have just been considering; the details of this discussion need not be rehearsed. It is particularly interesting, however, in this connection to note the recent endeavor to associate the development of malignant growths of the alimentary tract with trauma.* Once the ocular sarcoma becomes established a metastasis sooner or later occurs. All the organs may contain tumor masses, but certain of them are more prone to involvement than others. When there is a widespread dissemination, the distribution is much the same as that presented by our autopsy.

Almost all of the organs as above stated were involved. The spleen, bones, bladder, prostate and testicles were free from metastases. The pleuræ were extensively involved, but in the parenchyma of the lungs there were only two or three nodules about the size of a walnut and a few smaller masses just beneath the pleura. The tumor masses varied in color from a mottled grey to a deep black; the former usually firm, the more deeply pigmented portions almost diffluent.

Sections prepared from the abdominal lymph glands showed microscopically a pigmented large cell sarcoma.

The liver seems to offer a most favorable soil for the development of secondary growths, and it may be the only organ affected. Some of the largest livers on record belong to this group.

The liver of Litten's patient weighed about 10 kilo (27 pounds). In our second case the organ weighed 8.3 kilo (22 pounds). The capsule was tense and congested. Pigmented nodules projected from its surface, pushing the capsule out. At about the level of the umbilicus there was a fresh deposit of fibrin as well as old adhesions between the liver and the abdominal walls. There were similar deposits on the superior

*Boas. Deut. med. Wochenschr., No. 44, Oct. 1897.

surface of the right lobe and adhesions to the œsophagus. Projecting from the inferior surface of the right lobe near its lower margin was a pedunculated tumor 5 x 4 x 6 cm.; soft, lobulated and grey on section. Many nodules of various sizes were scattered through the substance of the liver; the largest about the size of an orange, black, and almost diffluent; the smaller variety usually greyish or slate color. Microscopically the pigmented tumor cells had an alveolar arrangement with scanty stroma intervening.

Assuming as we do that dissemination takes place through the blood, what determines the localization of metastases in certain organs and the escape of others is not at all clear. The same difficulty is met with in some cases of multiple lympho-sarcomata, and here it has been suggested that the process is really not to be regarded so much as a metastasis in the usual sense, but rather as an infectious disease, the result of the diffusion of a virus through the body (Schulz, Flexner). Efforts have been made to detect the materies morbi in the blood, but the results have not been encouraging. Pigment granules and pigmented leucocytes have been found, but actual tumor cells, as far as I know, have not been discovered.

The urine in cases such as we have been discussing often presents the condition known as melanuria. The urine of the second of our patients may be taken as an illustration of these phenomena.

On an average 1100 cc. were voided daily, of a brandy-brown color, with a specific gravity varying from 1008–1027; reaction, acid; neither albumin nor sugar present. At times polymorphonuclear cells and calcium oxalate were present in the flocculent sediment. Allowed to stand exposed to the air the urine became much darker, and the same change immediately ensued on the addition of an oxidizing agent (nitric acid, potassium bichromate). A solution of ferric chloride added to a specimen also caused it to turn black; diazo-reaction present.

The fact that the urine in melanosis is occasionally black has been long known, but it was not until 1858 that Eiselt accurately described the condition of melanuria in the case of a man suffering with "carcinoma" of the liver and eye. The urine darkened on standing, and the same change was produced by addition of nitric acid. The observation was verified, and from the character of the urine the opinion was ventured that the neoplasm was of a melanotic variety, an opinion which was later confirmed at the autopsy. To the hypothetical pigment the name melanin was given. The subject at once engaged the attention of the Prague school and many publications followed Eiselt's. In 1865 Dressler obtained an iron containing pigment from a melanotic growth of the liver, and about the same time Pribram separated by precipitation with neutral lead acetate a similar pigment from a melanuric urine. He concluded that the two pigments were probably identical. But later, in a brown pigment isolated from the urine of a patient with a melanotic growth in the orbit, Hoppe-Seyler could not demonstrate iron. In 1889 v. Jaksch added another reaction for melanuria, showing that ferric chloride even in dilute solution colored the urine black. He, like Pribram, found iron and also sulphur in the lead acetate precipitate. Almost simultaneously and independently of v. Jaksch, Pollak recommended a solution of ferric chloride as a delicate test for melanin. His analysis of the precipitated pigment showed besides sulphur and nitrogen, iron.

While melanuria was being investigated, attention had also been directed to the pigments of the sarcomata themselves. The results are not entirely in accord. The presence or absence of iron in the pigment is considered to have an important bearing on the question as to whether they take their origin from the blood. Whereas Berdez and Nencki report the pigment of sarcoma of liver and spleen as free from iron (phymatorhusin), Mörner reports an appreciable quantity. In this connection it is of interest to note that in their recent work on the pigment of negro's skin and hair, Abel and Davis point out that the difference of opinion regarding the iron content of melanin may be due to the fact that the distinction between the pigmentary granule and the pigment itself has not always been made. The granule contains iron, the pigment a steadily diminishing amount as it is more and more purified, so that finally only the faintest trace remains; from which they conclude that iron is not a constituent part of the melanin derived from the negro's skin. *A priori*, knowing that the choroid is so often the primary seat of melanotic sarcoma, one might expect a correspondence between the composition of "phymatorhusin" and the melanin of the choroid. But the fact is that while the former is rich in sulphur, in the pigment of the choroid there is neither sulphur nor iron.

Whoever has approached the subject of the melanins must have been impressed with the present unsatisfactory state of our chemical knowledge regarding them. In composition they approximate the proteids, and like them they present similar difficulties in separation and purification. The point of clinical importance, however, is that in melano-sarcomatosis the urine, as in Finkler's case, is sometimes black. More often, as in our case, it is clear when voided and becomes dark on exposure to air or on the addition of oxidizing agents. In the first class a melanin is excreted; in the latter group it is assumed that the melanin or phymatorhusin of the neoplasm is absorbed into the blood, is converted in the tissues into a colorless body melanogen, which is then excreted only to be reconverted into a melanin by oxidation. At what period in the course of the disease melanuria appears is not certain, but it is usually stated that a previous metastasis is necessary. We must look to the ophthalmologists for further information. Its diagnostic value, which might be considerable in an obscure case, is somewhat lessened by the fact that reactions similar to that of melanin-containing urine have been observed in some cases of peritonitis, of simple carcinoma of the stomach and liver, and following administration of tannic acid.

Finally, the question of the prognosis of melano-sarcoma of the uveal tract demands consideration. Left untreated, a metastasis sooner or later occurs. It is difficult to estimate the duration of the disease, for the ocular tumor is characterized at first only by ophthalmoscopic changes and its presence is not evident. Usually, after a period of one or two years, during which there have been more or less pain and functional disturbance of the eye, the tumor ruptures externally

and a metastasis occurs. The secondary deposits often grow with frightful rapidity and death soon ensues. Litten's case, in which the patient with a metastasis survived four years, is probably unique. The average duration of life is about three years. Widespread dissemination may have taken place before the neoplasm of the eye is suspected, and tumor masses in the liver, as in Litten's case and in Case I, may for the first time lead to a careful examination of the bulb. Early enucleation of the diseased globe has a certain prognostic import. In a study of 79 cases of sarcoma of the uveal tract whose after history could be followed, Lawford and Collins regarding patients apparently free from the disease more than three years after operation as well, report 25 per cent. of recoveries. Unfortunately, as they point out, no such limit can be fixed. Thus in Case II, although there was some evidence (abdominal pain) that metastasis may have taken place three years after the enucleation, yet it was not until nearly five years had elapsed that the patient presented himself with a local recurrence and an enlarged and nodular liver. Jonathan Hutchinson, Jr., cites a case in which the first evidence of metastasis appeared eleven years after the diseased globe had been removed. Such cases illustrate the gloomy outlook in melano-sarcoma of the eye, even when early enucleation is carried out; they make it impossible to say when an individual having had a primary ocular sarcoma can be considered safe from future trouble. It is comforting, however, to know that patients have been followed as long as sixteen and eighteen years after early removal without presenting signs of the disease.

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DISCUSSION.

Dr. ABEL.—The melanin, or black pigment, making up so large a part of the tumors in the case presented by Dr. Hamburger, is a substance of no little chemical interest. I wish merely to bring out two points relative to this pigment. First, the term melanin should be applied only to the black or brown pigments of the melano-sarcomata of the retinal and choroid coats of the eye, of the hair and skin, of the secretion of the cuttle-fish, etc.; in short, to a large class of substances which have been isolated by chemists, which are known to be stable and highly resistant compounds, possessing certain definite characteristics. The term should not be applied, as it sometimes is by histologists, to every brown or black particle which may be seen as a more or less temporary stage in the breaking down of red corpuscles in pathological conditions. A true melanin has not yet been isolated from an area where there has been an extensive disintegration of red corpuscles. We have no proof that the dark particles in such an area contain a genuine black pigment like the melanins.

My second point concerns itself with the origin of the melanins. Are they derivatives of hæmoglobin or of some other substance? Histologists have laid great stress on the iron content of a melanotic pigment, holding that the presence of iron lends great probability to the view that the pigment in question is derived from hæmoglobin. Now a micro-chemical iron reaction merely shows that iron is present in or on the *little particle* examined; it does not prove that iron is present in the *molecule* of the pigmentary substance to which the color of the particle examined is due. Iron may be present in the molecule of a pigment and yet micro-chemical methods may not be able to detect it, as in hæmatin, for example. Again, the pigmentary granule as deposited in cells is a very different thing from the pigment considered as a chemical individual; the former is a complex anatomical unit, containing many other substances in addition to the pigment. Confusion has resulted because this point has not been borne in mind. Davis and I showed that the pigmentary granules in the negro's skin and hair contained much iron, while the isolated and purified pigment contains none, and we have every reason for believing that this holds for every particle of melanotic pigment in the body. The fact is that much more than the presence of iron must be established before we can say that a pigment is derived from hæmoglobin. Some of the colored derivatives of hæmoglobin, as hæmatoidin, hæmatoporphyrin and biliribin, contain no iron, while the well-known hæmatin contains this element. Now all of these natural derivatives of hæmoglobin differ so widely in both their physical and chemical characteristics from the melanins, as thus far isolated, that no chemist can suggest a plausible theory for the derivation of these latter from the color-yielding complex of atoms in the hæmoglobin

molecule. To point out only one great obstacle, the melanins, with few exceptions, contain sulphur, the amount varying from 2 to 12 per cent., while the colored derivatives of hæmoglobin, like those already referred to, contain no sulphur. A theory of the origin of melanins must account for this difference and also for the difference in the carbon, hydrogen and nitrogen content, not to speak of physical differences as shown by the spectroscope. My own observations have led me to think of the sulphur-containing melanins, such as the sarcomelanin of this case, as highly altered proteids, as compounds that must still be classed in a broad way with the proteids. If, therefore, hæmoglobin is to be made the precursor of these pigments, it is the proteid part, or globin of the blood pigment, from which they are derived. But we can as easily suppose some proteid of the parenchymatous juices to be decomposed as that the proteid moiety of hæmoglobin should serve this purpose. We could assert with equal force that all the keratin in the body is derived from hæmoglobin.

Schmiedeberg has recently published the results of an elaborate research on the nature and origin of the melanins which bear out this view. I cannot go into the chemical details of the question, but can only give you his conclusions, to which I subscribe most heartily. The immediate precursor of the melanin is a product derived from a genuine proteid, say serum albumin, by a fermentative process; it is a highly resistant, modified proteid of the character, we will say, of an antipeptone which has lost carbon-containing groups, perhaps also leucin and tyrosin. This substance would therefore be richer in sulphur than the original proteid. It is further modified by having ammonia and water split off from it, its hydrogen content being further diminished by oxidation. These deductions are based on a careful comparison of the elementary formulæ of many proteids and of all of the melanins hitherto isolated and analyzed, and they harmonize entirely with the chemical processes known to occur in the body. No other rational theory of the origin of the sulphur-containing melanins, like those found in these tumors, in the hair and skin, etc., can be offered at present. I may remark in closing that the formation of the dark pigments seen in decaying vegetable matter, and which are called humus substances, presents many points of analogy.

ON INFECTION WITH A PARA-COLON BACILLUS IN A CASE WITH ALL THE CLINICAL FEATURES OF TYPHOID FEVER.

By Norman B. Gwyn, M. B., *Assistant Resident Physician, Johns Hopkins Hospital.*

Bacterial infection, or the intoxication caused by bacteria, gives to the blood the property of paralyzing and clumping the specific organisms. This is the principle of the Widal reaction, now so well known in connection with typhoid fever, and the same applies to other well-known organisms, such as the pyocyaneus and the bacillus of hog cholera. From this we may infer that a serum test is a valuable or certain proof of an organism's specificity. No better suggestion of this can be found than that shown by the colon family, in which Durham has shown that the serum of an immunized animal agglutinated decidedly only the organism used for the immunization, other colon organisms being but feebly affected. Widal infers from this that, especially in an infection caused by one of a group like the colon, the serum reaction is only of value as affecting that particular colon organism which has produced the infection.

For the production of this serum reaction in the blood of an individual, something more than the mere presence of the organism in the body is required. There must be a definite infection or intoxication produced before the blood will acquire its specific property. The presence of the colon bacillus in the normal intestine does not make it presumable that the blood of all persons will agglutinate the colon bacilli.

Based on the theory of specificity of the serum reaction, Widal* reports a case which he thinks (from the behavior of the patient's serum towards the organism isolated from his body) must be considered as an instance of infection by a para-colon bacillus, and the case he considers as one of para-colon infection.

The name para-colon is given to the organism as showing its resemblance to the colon family, but Widal gives it a place more properly between the bacillus typhosus and the colon bacillus, as its properties are closely allied to both.

The history of his case of so-called para-colon infection is as follows: A phthisical patient developed, after three weeks in the wards, an abscess in the neck about the œsophagus, showing at the same time some slight constitutional symptoms. From the pus at operation an organism was obtained in pure culture, actively motile, decolorizing by Gram; it did not liquefy gelatine, clouded bouillon without making a film, and formed a few gas bubbles in glucose agar; grew on potato as a yellowish green film.

The two most essential points distinguishing it from the colon family were that it produced no indol and did not ferment lactose, while the fermentation of glucose distinguishes it from the typhoid bacillus. Further reactions confirmed the fermentation of glucose and mannite, and the absence of the same in lactose and saccharose.

The main feature of the organism, however, was its serum reaction, and on this its claim of specificity rests. The serum of the patient had a marked agglutinative action on the organism in as high dilutions as 1–1000, the reaction diminishing steadily with convalescence.

To confirm this result various other organisms were com-

* Semaine Médical, Aug. 4, 1897.

pared. The different cultures of colon bacillus were affected by the patient's serum no more than by normal sera. Another para-colon bacillus isolated from the mouth agglutinated at 1–150; the bacillus psittacosis responded at 1–50. The serum of a guinea-pig inoculated with the particular para-colon organism gave no result with two colon bacilli, a typhoid bacillus and the other para-colon organism mentioned above. Conversely various normal sera and sera from patients with various affections. Sera of animals inoculated with different organisms had little or no effect upon Widal's para-colon bacillus, with the exception of typhoid sera of very high agglutinative power obtained by experimental inoculation. The sera of animals inoculated with colon bacilli, with the psittacosis organism and the other para-colon, gave little or no reaction on the organism.

Widal concludes from these serum reactions that the bacillus isolated was the cause of the patient's infection. The other para-colon bacillus referred to, isolated from a person's mouth, differed from that isolated from the abscess in fermenting saccharose in addition to glucose and mannite.

These two so-called para-colon bacilli, the psittacosis organism, a bacillus called the bacillus of calf septicæmia of Thomasson, Widal considers to form a family or group, in much the same way as the colon organisms are classified as a family. The individuality of the members is shown suggestively, though not absolutely, in the serum reactions mentioned above, and by differences in fermentation of the various sugars.

Recently we have isolated an organism which from its cultural properties seems to belong to this so-called para-colon group, and is possibly identical with one of Widal's para-colon organisms. It was found, moreover, that the patient's serum had a specific agglutinative power on the organism, and the conclusion was reached that the organism isolated had caused the infection. The case is of further interest as one of typical typhoid fever, and the question arises whether or not the organism found had produced a secondary infection during the disease.

Louis S., admitted Oct. 11th, 1897, had been ill since Sept. 17th with headache, fever and weakness, and later with vomiting, diarrhœa and pain in abdomen. On Oct. 14th noisy delirium set in; on Oct. 16th the patient had three hemorrhages from the bowel; he slowly rallied and went out in five weeks.

Rose spots were present; the spleen was palpable; the urine showed the diazo reaction; there was no diarrhœa. The temperature was that of a severe typhoid fever. There was never any Widal reaction found. Blood cultures on Oct. 12th gave a small, actively motile bacillus suggesting the bacillus typhosus. It decolorized fairly well by Gram, grew on agar as a grey blue moist raised film, clouded bouillon, giving no scum on surface and no precipitate. Milk was only faintly acidified, resuming original tint in course of ten or twelve days. Potato showed a brown yellow moist layer of growth. There was no liquefaction of gelatin, slight stab and surface growth. Plates of gelatin and of gelatin diluted with bouillon gave same circumscribed blue grey colonies, about ½ mm. in diameter; by microscope light brown regularly outlined granular colonies with no nucleus. The fermentation reactions showed fermentation of glucose, slight in saccharose, lævulose and mannite, but none in lactose. Sugar-free bouillon, to which in tubes 3 per cent. of various sugars was added, was used. There was no production of indol. By Van Ermengen's flagellar stain, from two to four flagellæ could be made out. No peritrichal arrangement as in the bacillus typhosus was seen.

The serum reactions were as follows: The patient's serum at different dates during his illness gave a rapid, complete agglutination in low dilutions, and showed reaction in dilutions up to 1–150 to 1–200, the highest being at date of discharge. On Dec. 18th, two months after date of culture, there still remains a slight reaction.

The same serum was without action on the bacillus typhosus in any dilution above 1–1 or 1–5.

Two varieties of colon were agglutinated by patient's serum as high as 1–50 and 1–60, but two normal sera agglutinated the same organisms in dilutions running from 1–60 to 1–100.

Typhoid sera of agglutinative strength ranging from 1–300 to 1–1100 were without effect on the bacillus in dilutions over 1–1 and 1–5. One typhoid serum, strength 1–900, with bacillus typhosus, gave an incomplete reaction as high as 1–30. Several of these sera had little or no effect even in dilution 1–1. One normal serum affected the bacillus rapidly at 1–1, failing at 1–5. A typhoid bacillus was affected similarly; a colon was agglutinated as high as 1–120; another normal serum had little or no effect at 1–1, while rapidly and completely agglutinating the colon organisms.

One other test mentioned by Widal for the distinction of the para-colon organism, is that called the scraped tube reaction, which consists in scraping off the surface growth of an organism from an agar slant and reinoculating with other or the same organisms. A fresh transplant of the same organism will not grow on the scraped surface; other different organisms will. Both colon and typhoid grow on the supposed para-colon tubes, and the para-colon grow on scraped tubes of them. Widal considers this an absolute distinction, stating that by it the different colon members can be distinguished.

The approach of the organism on the one hand to the typhoid bacillus and on the other to the colon family is well shown by the cultural properties. The effect on milk and the non-production of indol are like the typhoid bacilli; in the fermentation of glucose it resembles the colon family, from which again the non-fermentation of lactose and the negative indol test clearly exclude it. Its place really seems to lie between these two important organisms.

By comparing the cultural properties of our bacillus with those previously described, it can be seen that with the exception of the fermentation of saccharose the organism is precisely similar to Widal's para-colon isolated from the abscess; the resemblance to the one isolated from the mouth is more exact, as the latter had some effect upon saccharose. In the colon family, however, the fermentation of saccharose is a variable characteristic and may not occur with every member, so that this slight difference in fermentative quality may perhaps be a feature in the para-colon family as well. From these reactions and characteristics we think that the organism

here described may be considered a para-colon bacillus and may be identified with Widal's organism. Our infection unfortunately cannot be so clearly defined as his, occurring as it did in the course of typhoid, but if a serum reaction is a specific test, such an infection must have undoubtedly occurred. Of great interest, we think, is the fact that at no time, even up to the present, Dec. 18th, 1897, has the patient's serum given a Widal reaction, he being the only typical typhoid of 48 cases to fail therein, while his serum still shows after two months the result of the infection by the supposed para-colon organism.

THE MANAGEMENT OF SOLID TUMORS OF THE OVARIES COMPLICATING PREGNANCY, WITH REPORT OF A SUCCESSFUL CASE.

By William E. Swan, M. D., *Assistant Resident Gynæcologist in the Johns Hopkins Hospital.*

A careful examination of the literature shows that although solid tumors of the ovaries are not uncommon, their occurrence as a complication of pregnancy is sufficiently rare to justify a detailed report of every additional instance. Inasmuch, also, as the proper treatment of this condition is of the utmost importance, the following case offers certain points of interest.

A. R., single, white, domestic servant, aged 22, born in the United States, was admitted to the gynæcological wards of the Johns Hopkins Hospital, June 13, 1893. In the February previous (five months before) she had noticed an increase in size of the abdomen, which had gradually increased. Except for this enlargement of the abdomen, and amenorrhœa since January 1st, she had had no cause for complaint.

Family History. Paternal grandmother died of a new growth in lower abdomen. Maternal grandfather had a cancerous growth on arm; family history otherwise negative.

Personal History. Does not remember having had any serious sickness before. Menstruation began at fifteen; was irregular up to the 17th year, since then regular till 5½ months ago, of the 28-day type and of 5 to 6 days' duration; flow free; slight dysmenorrhœa.

Present Illness. Has always been healthy up to January, 1893. Early in February she first noticed a slight increase in the size of the abdomen, and absence of the menses, which have not returned since. The enlargement progressed in a symmetrical manner, and at the present time (June 3) the abdomen presents the appearances belonging to a five months pregnancy. The patient has had no morning sickness and has not noticed anything which could be interpreted as fœtal movements. There has been no increase in the size of, or pain in the breasts; no swelling of the feet or ankles. Sleeps well; appetite good; bowels constipated; slight giddiness; some dyspnœa on exertion; otherwise no inconvenience. No pain anywhere.

Physical Examination. General condition good. The patient is a well nourished, healthy-looking young woman; eyes clear, tongue slightly coated, mucosæ of a good color. Heart and lungs negative.

Abdomen symmetrically distended. Line of pigmentation from umbilicus to pubes marked. On light palpation a rather yielding, slightly resistant mass is felt extending from two inches above the umbilicus to the symphysis pubis, and from 3 to 4 inches to either side of the median line. On palpating deeply and quickly ballottement is obtained over this area, showing the presence of a layer of fluid. The abdomen over the same area is dull on percussion; on auscultation a placental bruit is heard in the right lower quadrant of the abdomen; no fœtal heart sounds are heard; no actual movements made out, but indefinite "lumps" are felt through abdominal wall which "retreat" from the examining hand.

The measurements of the abdomen were as follows: Girth at umbilicus, 30 inches; girth midway between umbilicus and symphysis, 31 inches; from the ensiform cartilage to umbilicus, 7⅞ inches; from the umbilicus to the symphysis, 7¼ inches; from anterior spine of ilium on either side to umbilicus, 6½ inches.

Vaginal Examination. Vaginal mucosa dusky violet in color; outlet considerably relaxed; cervix high up, soft, shortened, patulous. Behind the cervix and occupying a large part of the pelvis is a hard, nodular, fixed mass, about 5x7 cm. in diameter, adherent to sacrum posteriorly. The breasts contained colostrum.

Diagnosis. Pregnancy, associated with solid tumor of the left ovary.

Abdominal section by Dr. Kelly, June 21, 1893.

Incision 18 cm. long through stretched and thinned abdominal walls. The uterus, which was of the size belonging to a five months pregnancy, was forced out by compression made on the sides of the abdomen by the hands of an assistant, the operator meanwhile making direct traction on it and throwing it forward so that the body rested on the pubes. By these means there was brought into view a tumor of the left ovary, lying behind the uterus in the pelvis but not attached to it. It presented a whitish appearance, was hard, irregularly oval, and about the size of two clenched fists placed closely together. Pressure upon it had caused some flattening of the surface adjacent to the sacrum. The tumor, which was attached to the left broad ligament by a narrow pedicle, was raised and tied off together with the left tube by means of four intermediate silk ligatures, a few extra silk ligatures being inserted to stop some slight oozing from the severed pedicle. The uterus, which had all this time been protected by means of a large piece of gauze kept constantly saturated with warm salt solution, was now returned to the abdomen. The peritoneum was united by means of a fine silk suture; the remaining layers of the abdominal coverings with silk-

worm gut and silk; gauze dressing, edges rendered adherent with collodion; iodoform and boric acid powder dusted over same; cotton; Scultetus' bandage.

Time of operation 46 minutes.

The convalescence was rapid and uneventful; the highest temperature reached was on the second day, when it rose to 101° F., after which it soon became normal; the bowels moved on the fourth day. On July 2, 1893 (12th day), note reads: "For the first few days after operation a slight bloody vaginal discharge was observed; patient complained of sharp pains through the abdomen. This symptom soon subsided under a moderate use of morphine. Abdominal dressings removed; wound united throughout *per primam;* general condition excellent."

July 10, 1893 (20th day), "Patient sat up in bed; did not feel weak nor tired afterwards."

July 22, 1893 (4 weeks after operation), "Patient discharged; has had no setbacks; wound nicely healed; patient feels well; abdomen increased in size."

Pathological Report. Mass consists of a large tumor developed from left ovary, with about 4 cm. of normal tube, with clear mesosalpinx; tube patulous. Tumor 12x7 cm., density of cartilage, with clear smooth fibrous capsule, which strips off moderately easily. On outer surface is an umbilication about 3 cm. deep, containing a small mass of similar consistence, with broad flat pedicle. Vessels on surface small but injected. Section of mass reveals a dense fibrous structure, yellowish and translucent, with numerous deeper pinkish areas corresponding to umbilication on surface; tissue much softened, and upon pressure exudes a clear fluid.

Frozen sections reveal fibrous tissue with fine points of fatty degeneration.

Sections hardened in alcohol. The specimen consists of dense fibrous tissue with spindle-shaped nuclei. The tumor is richer in cells in the larger portion. The capsule is much thickened. Vascular supply scanty, especially around the umbilication. Diagnosis: Fibroma of ovary.

From the after-history it would seem clear that premature labor was artificially induced after the patient returned home. When she left our care she was certainly well, and had nature been left to herself there was nothing in the patient's condition to prevent the continuance of the pregnancy to term, and there was no indication that in this case delivery would have been accompanied with any more danger than that belonging to a normal labor.

Considerable confusion seems to exist in the minds of authors regarding the classification of tumors of the ovaries associated with pregnancy. In many reports of cases of ovariotomy during pregnancy, only incidental reference or none at all is made to the nature of the growth removed. Thus, J. Dsirne[1] (Liveland) collected from the literature 135 cases of pregnancy associated with ovarian tumors in which ovariotomy was performed, the diagnosis in 42 of these being tumor ovarii, and in the remainder cystoma. None are distinctly specified as being solid tumors.

Most tumors of the ovary, including those complicating pregnancy, are cystomata, and of these dermoids form a considerable number, as is shown by the following table:

Name of operator.	Total number of cases operated on.	Cysts, including dermoids.	Number of solid tumors.	Fibromata.	Sarcomata.	Carcinomata.
1. Billroth	86	78	8	..	3	5
2. Schroeder	102	97	5	..	5	..
3. Thornton.....	338	328	10	3	..	7
4. Hildebrandt..	37	27	10	..	..	..
5. Weber.....	123	72	51	..	..	..
6. Krassowoski..	128	128	..	..	..	..
7. K. Von Brann.	81	71	10	1	2	5
8. Thos. Keith ..	200	183	17	..	..	..
9. Olshausen	193	267	26	6	9	5
Totals	1388	1251	137	10	19	22

The figures in the above table give, as we see, 9.9 per cent. solid tumors. But Olshausen[2] holds that this is too large a proportion. Weber, whose statistics tend materially to raise this percentage of solid neoplasms, has probably counted as solid tumors many which other authorities would class among the cystic variety. With Weber's cases omitted we should have only 6.8 per cent. of solid tumors, which is probably more correct.

The same table shows the relative frequency of the different varieties of solid tumors to be as follows:

Fibromata	are	present	in	the	proportion	of	.72 per cent.
Sarcomata	"	"	"	"	"	"	1.36 "
Carcinomata	"	"	"	"	"	"	1.58 "
All others	"	"	"	"	"	"	.057 "

The investigations of Jetter[3] have shown that any form of ovarian tumor may complicate pregnancy. Of his collection of 166 cases, 97 were cystomata, 37 dermoids, 11 carcinomata, and 21 uncertain. In this small number of cases the proportion of undoubted solid tumors to all others is only 6.6 per cent.

Solid tumors of the ovaries may be classified as follows:

- Solid
  - Desmoid
    - Fibromata,
    - Sarcomata,
    - Myxomata,
    - Endotheliomata,
    - Enchondromata.
  - Epithelial
    - Carcinomata,
    - Papillomata.

The lines between these several varieties of tumors are not always distinctly drawn, and almost any two forms may be found associated. The benign forms of epithelial tumors of the ovary are always cystic in nature (Olshausen[4]).

Ovarian neoplasms do not preclude the possibility of conception so long as the ovaries contain healthy ovarian tissue. Indeed, rare instances have shown that the removal of both ovaries is not an absolute safeguard against conception. In such cases there are undoubtedly rudimentary masses of ovarian tissue or supplementary ovaries left behind (Montgomery[5]).

It is difficult, if not wholly impossible, to arrive at any accurate conclusions as to the frequency of conception in women who are the subjects of ovarian neoplasms. S. Remy[6] finds, however, that in 257 women with tumors, 321 pregnancies occurred, with 266 normal deliveries; so that some of the

mothers became pregnant at least twice during the existence and probable growth of the same tumor.

Montgomery, in commenting on the frequency of ovarian tumors complicating pregnancy, says he is able from a very cursory investigation of the literature to present tables of over 150 cases. It is evident that he refers to cysts of the ovary associated with pregnancy.

Several authors, as Kleinwächter, Spencer Wells and Rokitansky, have observed pregnancy in connection with unilateral ovarian fibromata. During labor the tumor may obstruct the birth canal, and thus render Cæsarean section necessary, as happened in Kleinwächter's case; the tumor may be contused and become gangrenous, as has been described by Rokitansky.[7]

After a careful examination of the literature we have been able to find but fourteen cases of undoubted solid growths of the ovary in association with pregnancy. These are here presented in chronological order with brief histories.

Case I. Breit[8]. In this case an ovarian tumor of stony hardness and adherent to the rectum was removed; no details given.

Case II. Spiegelberg[9] (reported by Bourgonin). Patient was aged 37 and had borne two children. Immediately after the birth of the second child a rapid enlargement of the abdomen was noticed, which pursued a slowly progressive course and ended in death. At autopsy a fibroma of the left ovary weighing 60 pounds was found, with considerable ascites. Size of tumor 51x23 cm.

Case III. Spiegelberg[10] (reported in 1867). The woman died nine days after her second labor, aged 36. Tumors of both ovaries were found at autopsy which microscopic examination showed to be myxosarcomata which had undergone cystic degeneration. One tumor measured 20x12x4 cm.; the other 15x10x4 cm. Death was due to rupture of one of the tumors, apoplexy of both, and peritonitis.

Case IV. Kleinwächter[11] reported in 1872 the following case. Age of patient 31 years; month of pregnancy not stated, probably full term; pains began on May 25, and on May 29 were very severe. Patient was brought to the hospital by midwife, who got away before giving any further information. Head presenting. Examination revealed a bony tumor, about the size of a fist, in the pelvis. Cæsarean operation performed on May 31, 1868, and a healthy female child weighing 3010 grammes safely delivered. Twenty-five hours afterwards the mother died of general peritonitis.

Diagnosis. Peritonitis after Caesarean section; ossified fibroma of the right ovary.

Case V. Spencer Wells[12] (reported by Cayla). The patient, aged 29, who had had one child, presented herself in March, 1872, with a tumor in right suprapubic region. She was three months pregnant. One month later laparotomy was performed, and a tumor weighing five kilograms was removed. This tumor had been held in place by the epiploon to which it was adherent. The structure of the tumor was that of an œdematous fibroma. The patient recovered and the child was born at term.

Case VI. Hempel[13] in 1875 reported the case of a patient aged 42 who died four weeks after her 11th labor. At autopsy both ovaries were found enlarged to more than the size of a child's head. The surfaces of the tumor masses were hard and irregular. The tumors proved to be carcinomata, probably secondary to cancer of the stomach.

Case VII. Schroeder[14] (reported by Cayla). Woman aged 22, six months pregnant; operation May 25, 1876; solid tumor removed from left ovary. Labor at term; cure.

Case VIII. Spencer Wells[15] (reported by Cayla.) Woman aged 41, four months pregnant; operation October, 1876; tumor weighed 7 pounds. Labor at term; cure. Diagnosis: Round cell sarcoma of left ovary.

Case IX. Spencer Wells[16] (Cayla). Woman aged 28, four months pregnant; operation November, 1877. Fibroma of right ovary removed, weighing 10 pounds. Labor at term; cure.

Case X. Casati[17]. Large fibro-sarcoma of left ovary. Pregnancy at fourth month. Ovariotomy; abortion, partial suppurative peritonitis; cure. Patient was 29 years old. Menstruated at 18; married at 25; ten months later had first child. In March, 1881, had second child; labor normal. Two months after this noticed tumor in left groin. Four months after labor menses recommenced; milk stopped at 5th month. On January 4, 1882 (ten months after birth of last child), the patient was examined and the following diagnosis made:

Completely solid tumor (probably sarcoma) of left ovary; partial peritonitis and pleurisy. At operation the woman was found to be four months pregnant. The tumor weighed 1850 grammes, and measured 13x48x36 cm.

Case XI. Dr. J. H. Carstens,[18] of Detroit, Michigan, in 1889 reported a case almost identical with our own. The patient, aged 26, white, four years married, without having had children or miscarriages, had had frequent micturition and pain for the year previous. She had noticed a hard lump in lower abdomen, which had increased rapidly during the last four weeks. The menses, which had formerly been regular, ceased February 24, 1889. General health and family history good. Examination showed the pelvis to be filled with a hard growth which seemed movable. The uterus was found a little to the left of the growth. The os was soft, velvety. Pregnancy suspected. Examination under ether warranted a diagnosis of pregnancy of two months duration and a pelvic tumor, which was thought to be a uterine fibroid with a long pedicle, a sarcoma, or some other hard tumor of the ovary. Operation May 27, 1889. When the peritoneum was opened a very hard nodular tumor came into view. It was movable, slightly adherent to the bladder, intestines and omentum, but not adherent to the uterus. The long narrow pedicle was tied off together with the right Fallopian tube, which was also removed. The left ovary was found to be healthy and was left untouched. Patient made a good recovery. The pregnancy continued and was of seven months duration at the time the case was reported. The tumor was very hard and nodular, 10 cm. long and 12 cm. in diameter; in the middle was a constriction in which the uterus had rested. A microscopical examination by Dr. George Duffield showed only pure fibrous structure. The ovary had entirely disappeared in the growth.

Case XII. Münchmeyer[19] (reported in 1890). Patient aged 30. Third pregnancy. Month of pregnancy not stated, probably full term. Normal but small pelvis. Enormous elastic tumor (spindle-cell sarcoma) occupied the pelvis. Head presenting. Shortly before the delivery of fœtus the colossal swelling of the tumor was noticeable. The absence of any symptoms pointing to malignancy of the tumor was noted. The child being already dead, the skull was crushed and the fœtus delivered. The tumor remained for four weeks after the delivery, but shrunk to about the size of a goose egg(?). Ovariotomy was then performed; the patient made a good recovery, and was discharged three weeks subsequently.

Case XIII. J. Murphy.[20] Abdominal section during pregnancy (reported in 1895).

"A lady 32 years old was sent into the Sunderland Nursing Institute, under my care, to have an ovarian tumor removed, she being about six months pregnant. The operation was performed at noon, April 20, 1893. The tumor proved to be a solid round-cell sarcoma, weighing two pounds, with somewhat numerous adhesions. The labor pains commenced 24 hours after the operation and became severe at 10 a. m. The patient soon gave birth to a boy, who lived for 12 hours. The convalescence was uneventful. She left the Institute in three weeks. Her highest temperature was 99.5° F."

Case XIV. P. Ruge.[21] Woman aged 36; six months pregnant. Myxo-sarcomata of both ovaries; no details.

From an examination of the results in the above fourteen cases we find that eight of the patients were submitted to operation before labor, with the death of one mother and with loss of but two children from miscarriages and one by craniotomy, four children going to full term and one being delivered by Cæsarean section. Three mothers were not operated on; of these, two died soon after labor as a result of complications due to the tumors, and one lived; in three cases no details are given.

The incompleteness of the above collection of cases is painfully apparent. A glance at the various dates of their publication—1861 to 1895—would suggest at once that many similar cases must have occurred previous to the former and probably also subsequent to the latter date. Their non-appearance either in the Index Catalogue of the Surgeon-General's Library or the Index Medicus, would lead to the conclusion that such instances were either not reported at all, or that the accounts of them did not possess sufficient detail and clearness to enable the cases to be recognized as belonging to this category. So-called solid dermoids and all other tumors not distinctly specified to be solid have been rejected from our list.

Influence of Pregnancy on the Growth of Ovarian Tumors.

In this connection two main theories may be cited: (1) That the increased blood flow increases the growth of the tumor (Spiegelberg and Olshausen). (2) That a decrease in the size of ovarian tumors during pregnancy occurs, owing to lack of space and inactivity of the ovaries (Koeberle). The former of these two views is generally accepted (Dsirne).[22]

Wernicke suggested that benign tumors are apt to become malignant during pregnancy. There are no observations which tend to support this view (Olshausen).[23]

Löhlein[24] in 1895 published a comprehensive article dealing with ovarian tumors complicating pregnancy. His views may be summarized as follows:

(1) He dissents from Wernicke's view and holds that benign tumors of the ovary do not tend to become malignant during pregnancy. (2) He doubts if tumors enlarge much during pregnancy and cites cases to support this position. He quotes many observations to show that the ovaries are in a state of rest during pregnancy.

The recognition of the co-existence of pregnancy with a solid ovarian tumor or tumors is of the greatest importance, and often presents a difficult problem. The limits of this paper forbid more than a brief discussion of the main characteristics of this condition.

Solid tumors of the ovaries are often bilateral, though there are many exceptions to this rule; they are seldom larger than a man's head; the general form of the ovary is maintained; adhesions are rare, but ascites is usually present (Olshausen).[25]

Although the signs and other evidences of pregnancy, in association with solid tumors of the ovaries, are sufficiently characteristic, it is a noteworthy fact that many experienced and able operators have recognized the pregnancy only after the abdomen has been laid open. It is therefore not out of place to emphasize the importance of keeping in mind the possibility of the existence of such a condition in making our examinations.

In this connection it is interesting to note that Napier,[26] after reporting a case of ovarian cyst in which he successfully performed cystectomy at the third month of an unsuspected pregnancy, quotes from Barnes' "Diseases of Women," as follows: "Ovariotomy during pregnancy has been performed several times, the operator not suspecting the existence of pregnancy before the operation. What should be done when a pregnant uterus is discovered during some stage of ovariotomy? Wells says let it (*i. e.* the uterus) alone. Dr. Atlee performed ovariotomy in the second month of an unsuspected pregnancy. Dr. Marion Sims performed ovariotomy in the third month of pregnancy, not suspecting its existence, with good results to mother and child."

The prognosis in cases of ovarian tumor complicating pregnancy is by no means favorable. The great danger to the mother will be appreciated from the figures in the following statistics.

Litzmann has collected 54 cases with 24 maternal deaths; Jetter, 215 deliveries in 165 mothers with 64 deaths; Playfair, 57 deliveries with 23 deaths; Braxton Hicks, 6 deliveries with no deaths; Rogers, 5 deliveries, no deaths; Spencer Wells, 11 deliveries, one death; Fritsch, 4 deliveries, one death. In all, 355 deliveries are reported with 114 maternal deaths, or a maternal mortality of about 32 per cent. The mortality to the children from either abortion or premature labor is, according to Engstrom, much greater. In 216 cases he finds it to be about 48 per cent. (Fenger).[28]

Heiberg[26] has collected 271 cases of pregnancy with ovarian tumors and found that over one-fourth of the mothers and two-thirds of the children perished; while Dsirne[27] says that only 60 per cent. of the pregnancies complicated by ovarian tumors terminated without accident to mother or child.

The situation and size of the tumors are of marked significance in determining the prognosis. Most solid tumors, especially during their early growth, remain in the true pelvis. When small they may be overlooked, and the hindrance which they offer to delivery may be unsuspected or attributed to pelvic narrowing (Montgomery).[29] Large tumors rarely hinder the engagement of the fœtal head, unless a part of them occupy the pelvis; whereas small tumors, especially dermoids, often retard the descent of the head, so that operation is necessary (Hohl).[29]

Greigg,[30] from his post-mortem researches upon puerperal septicæmia, shows that it is possible that some cases of this disease arise from injury, during parturition, to unrecognized ovarian tumors. We must consider not only the mechanical difficulties in the way of delivery, but also the cachexia due to the presence of malignant new growths (Müller).[31]

Complications of pregnancy may arise owing to the presence of solid ovarian tumors.

1. The stem of the tumor may become twisted and thus give rise to the presence in the abdominal cavity of a necrotic foreign body. This accident occurs in 9.1 per cent. of all cases (Dsirne).[32]

2. Infection of the peritoneum is more likely to occur.

3. The tumor by direct pressure on the intestines may

cause intestinal obstruction, or indirectly twists of the gut or hemorrhoids (Barsony).[33]

The mortality in ovarian tumor cases complicating pregnancy, treated by the expectant plan, is frightful. In 75 cases (cysts included) collected from the literature, 31, or 41 per cent., were fatal to the mothers, while but 22 children, or 29 per cent., are reported as having been saved (Montgomery).[34]

Litzmann[35] gives the maternal mortality as 43 per cent., and the fœtal as 83 per cent.; while Dsirne, as stated above, reports that but 60 per cent. of these cases when left alone terminate without accident to mother or child.

Such a death rate urgently demands renewed investigation and the adoption of a definite plan of treatment. When we come to the consideration of ovariotomy during pregnancy, we find far better results.

Of cases of ovariotomy during pregnancy, Dsirne finds that abortion followed in 22 per cent., and death in only 5.09 per cent. Breit[36] (1861) reports results of operation on tumors of the ovary in pregnancy during labor, or the puerperium, as follows: In 215 cases, 140 mothers recovered, 64 died; in 11 the results were unrecorded. Of the children, 81 lived, 53 died, of 61 there was no record; 21 abortions occurred.

So far as the chances of maternal recovery from ovariotomy during pregnancy are concerned, they are fully as good as when no pregnancy exists. As regards the continuance of gestation, if the operation is performed in the early months the prospect is usually also favorable (Mundé)[37]

In this connection Kreutzmann[38] states the facts clearly when he says: "The bringing about of abortion would be in order (1) if it is proved that ovariotomy during pregnancy is always followed by abortion; and (2) if the statistics show that the results of ovariotomy in pregnant women are much less favorable than in non-pregnant women. The fact that the percentage of abortions following operation is only about 20 per cent. is an answer to the first proposition. As concerns the second, statistics have demonstrated that with most operators the mortality in ovariotomies performed during gestation is less than those in non-pregnant women."

Since ovariotomy, then, can give such good results, the advisability of operative procedures must be taken into consideration in each individual case. Surgeons of wide experience, as Spencer Wells, Tait, Cauchois, Olshausen, and the late Carl Schroeder, are agreed in commending ovariotomy as the best means of dealing with all cases of ovarian neoplasms associated with pregnancy. Again, in view of the fact that Cohn[39] has proved every sixth ovarian tumor to be probably malignant, the early removal of the diseased structures is of vital importance.

The most favorable time for operation is at some period during the first half of pregnancy. In the later months the increased hyperæmia and engorgement of the broad ligaments increase the danger of untoward results (Montgomery).[40]

Kelly has published statistics which go to show that all tumors of the ovary should be extirpated as soon as recognized, no matter how small or inoffensive they may appear. His experience with cysts of the ovary has clearly demonstrated that it is not safe to allow them to remain, inasmuch as many apparently innocent cysts (papillary cystomata) may at any time become highly malignant, and if not removed sufficiently early, may prove rapidly fatal.

According to Olshausen,[41] from 60 to 70 per cent. of all patients with proliferating cystomata (cystoma ovarii proliferans papillare) die within three years from the time of the first symptoms, and a further 10 per cent. die during the fourth year.

This surgical law which insists upon the early extirpation of all ovarian tumors applies with still more force in cases of solid ovarian neoplasms associated with gravidity.

Time for Operation. The elective time for the operation seems clearly defined, as all agree that the lowest mortality to both mother and child is secured by operating between the second and fourth months of gestation. There is one apparent exception to this rule. Dsirne[42] states that in intra-ligamentary tumors, owing to the danger of hemorrhage, it is often better to produce abortion before extirpating the tumor. It may, however, be asserted that the results in these particular cases will be determined largely by the skill and operative dexterity of the surgeon, and that under favorable conditions these cases can also be successfully operated on without previous interference with gestation.

When the case is not seen before labor, and when the tumor interferes with the engagement of the head in the true pelvis, one or both of the following procedures are indicated:

(a) Attempts may be made to replace the tumor in the abdominal cavity under anæsthesia.

(b) As a last resort, celiotomy.

In the puerperium Hohl[43] says that we should operate not later than the second week. Others hold that if the labor is normal it is better to wait several weeks longer.

In summarizing the results of a thorough search of the literature dealing with the subject the following deductions would appear to be justifiable:

I. Solid neoplasms of the ovary complicating pregnancy are exceedingly rare.

II. The diagnosis of this rare combination of a physiological and pathological process may be very difficult. In certain cases much help can be obtained from recto-abdominal palpation under narcosis, using Kelly's method to gently produce artificial descensus of the uterus. The physical examination with the signs of pregnancy, and those which belong more particularly to solid ovarian growths, will generally enable us to make at least a probable diagnosis and one sufficient to warrant an exploratory section.

III. The prognosis in cases of solid growths of the ovary complicating pregnancy is much worse, both for mother and child, than in those of cystic neoplasms of these organs. This is to be explained by the fact that the former are usually smaller and remain in the true pelvis and obstruct the parturient canal, while the latter, owing to their bulk and consistence, rise above the pelvis, and the dystocia, if produced at all, is of a less serious nature.

Abdominal section and extirpation of solid tumors during the early months of pregnancy produce equally good results, so far as the life of the fœtus is concerned, as in the case of cysts; the ultimate result in the case of the mother depending,

of course, on the malignant or benignant nature of the new growth.

IV. In the management of these cases we have seen that if the extirpation is undertaken during the elective period of gestation (second to fourth month) the maternal mortality was but 5 per cent., due to hemorrhage, shock, sepsis, and other causes; whereas the fœtal mortality due to abortion is only 20 to 22 per cent. as compared with 40 per cent. for the former and 80 per cent. for the latter when these cases are left to unaided nature.

The general rule, then, should be to operate on all cases between the second and fourth months of gravidity. It would be hard to find a stronger argument in favor of the elective operation for extirpation of these ovarian neoplasms than is furnished by a comparison of the statistics of the best authorities.

V. The compulsory operation (during the latter half of gestation, during labor, or the puerperium) will rarely be required. One then should be guided by the suggestions of Hohl, preference being given to the procedures in the order above mentioned.

In conclusion I desire to express my deep sense of obligation to Professor Kelly for permission to report this unusual case; to Dr. Cullen for much encouragement and assistance in obtaining references; and to Dr. Bardeen for valuable aid in abstracting literature.

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THE CATHETERIZATION OF THE URETERS IN THE MALE THROUGH AN OPEN CYSTOSCOPE WITH THE BLADDER DISTENDED WITH AIR BY POSTURE.

By H. A. Kelly, M. D., *Gynecologist-in-Chief to The Johns Hopkins Hospital.*

The difficulties and the dangers of the various devices for electric cystoscopy with the source of illumination introduced within the bladder are so great that I feel sure urologists everywhere will welcome and test carefully any new method of examination which bids fair to limit or to supplant these methods by one which is simpler, more direct and more satisfactory in its results.

I have succeeded in devising such a method and in demonstrating its utility in the presence of an audience of expert urologists and surgeons at St. Luke's Hospital, New York City, Feb. 4th, 1898, through the kind invitation of Dr. L. Bolton Bangs, consulting surgeon, and the courtesy of Dr. Robt. Abbe, visiting surgeon, who offered me his clinic hour.

Among the visitors present were Drs. Robt. F. Weir, Willy Meyer, Clement Cleveland, Robt. A. Murray, Farquhar B. Curtis, F. Tilden Brown, and others.

I was greatly indebted to the house staff of the hospital for their warm, intelligent interest and assistance throughout.

Dr. Otto G. Ramsay accompanied me from the Johns Hopkins Hospital and aided me skilfully at every step of the investigation.

The cystoscope used was a straight metal nickel-plated tube 15.5 cm. long, 7 mm. in diameter, the caliber being equal from end to end, except at the conical external orifice, which measured 2.7 cm. at its outer border and was blackened on the inside to prevent the reflection of the light from obscuring the field. A stout handle 10 cm. long was attached to the outer end.

The source of illumination was a small electric headlight, deriving its current from the house supply, reduced by a Vetter controller.

The patient, a young man, was put under Schleich's anesthetic, when I introduced the cystoscope armed with its obturator as far as the prostate, and then guided it easily over the prostate and into the bladder by raising and guiding the end with one finger introduced into the rectum. The penis, of average size, shortened on the cystoscope to a length of about 5 cm.

He was then carefully turned over and placed in the knee-chest posture and brought to the edge of the table and the obturator withdrawn; air at once entered the bladder and the investigation was made.

The light was good and the base of the bladder at once came clearly into view; the posterior wall was seen by elevating the handle a little, then by turning it to the right and to the left the left and right lateral walls were clearly seen. I then withdrew the speculum until the internal urethral orifice began to close over it, and then pushed it in a little, turned it about 30 degrees to the left and dropped the handle, when the right ureteral orifice came clearly into view, as clearly as I have ever seen it in a woman.

Dr. Willy Meyer looked through the cystoscope and agreed it could not have been seen clearer or more unmistakably if it had been on the surface of the body.

Dr. Ramsay then handed me one of my renal catheters, 50 cm. long and 2 mm. in diameter, armed with a stylet, and this was guided, after two attempts, up into the ureteral orifice, and easily stripped of the stylet, into the ureter, ascending up to the pelvis of the kidney. Dr. Abbe now looked through the cystoscope and saw the catheter entering the bladder wall.

The patient was then put to bed with the catheter in position, and before leaving the hospital I had the satisfaction of knowing that half a test-tube full of slightly cloudy urine had been collected.

By this method of cystoscopy not only is the diagnosis of vesical lesions simplified, but simpler and direct plans of treatment, such as curetting, cauterizing and making applications to localized areas are made possible. Small tumors may also be easily excised or snared.

A preliminary note has been published in the *Annals of Surgery* (Jan. 1897), where a fuller account will shortly appear.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of December 20, 1897.

Dr. Barker in the Chair.

On Super-Arterial Pericardial Fibroid Nodules.—Mr. Knox.

In 1866 Kussmaul and Maier reported an instance of the development upon many of the smaller visceral arteries, of nodules, to which condition they applied the name of peri-arteritis nodosa. Since this time additional cases of a similar disease have been described by Chvostek and Weichselbaum, Meyer, Fletcher and Von Kahlden. This rare condition is characterized by the presence upon the smaller arteries, except those of the brain and spinal cord, of small grayish-white nodules, which microscopically are found to be associated with hypertrophy of the internal and adventitial coats of the affected vessels, and with weakening or even rupture of the middle coat. The origin of this affection is conceived to be either some form of infection or intoxication.

Some months ago my attention was directed, through the kindness of Dr. Flexner, to a heart which showed upon its surface, over the arteries, opaque elevations suggesting those of

peri-arteritis nodosa. Later, at the autopsies, several other hearts affected in like manner were found, and I was permitted to study the specimens in the Pathological Laboratory.

The extent of the process varied, from tortuous, more or less uniform elevations over the arteries, to whitish dots, minute in size and few in number, which almost escape attention.

The elevations may be separated from each other by wide intervals, may be quite close, resembling beads strung along the vessel, or they may coalesce throughout the entire length of the artery.

The nodules were found exclusively upon the ventricles and the interventricular septa; never within the heart muscle, upon the auricles, nor over the veins. They were never noticed elsewhere in the body.

On microscopical examination there were no constant alterations to be made out in hæmatoxylin and eosin stained specimens in any of the arterial coats, but between the adventitia of the vessel and the surface there was a marked fibrous thickening projecting beyond the level of the pericardium and producing the nodules seen in gross specimens. At the base of the nodule and at the sides lymphocytes and a small number of polymorphonuclear leucocytes were accumulated.

The appearance in cross-section was as though a compact mass of firm connective tissue, convex on its inner surface, had been placed upon the artery in the loose pericardial tissue.

The nodule may be only a small oval patch over a portion of the artery, or it may extend a considerable distance upon each side.

The earliest stages of the process met with showed simply a serous infiltration and an accumulation of small round cells superficial to the artery on its outer side.

In no case was any tendency to fibrous formation noticed on the inner side of the vessel, next to the heart muscle, nor in the heart muscle itself.

The constant relationship of the fibrous thickenings to the arteries suggested that the nodules were in some way associated with changes in the arterial walls not brought out by the stain in hæmatoxylin and eosin, and a representative number of the sections were stained for elastic tissue by the fuchsin method described by Manchot.

There were of course variations in the sections, but the results were sufficiently uniform to be quite suggestive. In a few sections there were distinct breaks in the inner elastic coat just opposite the nodule, but the most noticeable alteration and the one present in most of the preparations was a diminution in the strength of the *outer* elastic coat between the muscle and the adventitial layers.

This membrane was well represented on the inner side of the artery often by a heavy dark red band, but as one approached the outer half it became thinned, the fibers looser and separated from each other until usually just beneath, at times a little to one side of the fibrous thickening, only a few straggling strands of the elastic fiber remained.

In no instance was this change accompanied by an increase in the thickness of the inner elastic coat. Occasionally only were defects in either elastic layer seen on the inner side of an artery. In these cases no alterations corresponding to the nodule under discussion were present in the remaining layers nor in the surrounding tissue.

The change described was not seen in arteries not surmounted by the fibrous patch.

These findings would suggest at least some association between the nodules on the surface and the weakening in the arterial wall beneath.

The affection, as far as can be ascertained, was discovered incidentally in every case, and produced no symptoms as far as can be known.

From the above description there can be no doubt that the condition found in the epicardium of these cases is entirely distinct from peri-arteritis nodosa. There was, too, nothing in the histological appearances that was suggestive of a primary bacterial or toxic action upon the tissues leading to the fibrous formation, and the bacteriological studies of the cases at autopsy did not support such an assumption.

In considering the histological appearances one is tempted to regard the changes in the elastic coat as the primary alteration. Moreover, a number of facts in the protocols lend support to this idea, for the individuals in whom the condition was found were subject to unusual strains put upon their cardio-vascular system.

Of four cases in which the nodules were present, three showed heart hypertrophy. In one, lesions of the valves existed; in another, arterio-sclerosis. Three of the cases suffered from nephritis; in three there was œdema, and in one case aneurism. Three of the four patients gave histories of heavy work, irregular life, and the ingestion of large amounts of alcoholic beverages.

Discussion of Dr. Hunner's Cases of Aneurism (*continued*).
See February BULLETIN, p. 38.

Dr. OSLER.—The most interesting thing about this case relates to the diagnosis. This patient was under observation last year, and there were several points of great interest at first which made us doubt whether he really had aneurism of the aorta. We could not grasp a very positive tumor. There were well-marked pulsation and a definite thrill and murmur, but these, in the absence of a tumor, when you have reached a certain grade in your experience, are insufficient. He had aortic regurgitation, but that also made us hesitate, for you know how frequently, particularly in young persons, great dynamic pulsation is present. He was under observation for many months, and several additional features came out which made the diagnosis of aneurism of the aorta reasonably certain. In the first place the characters of the pains, that had kept up in a very persistent way and required a great deal of morphia to relieve. Then he developed a loud bruit at the back; but what really clinched the diagnosis was a pulsation at the back which could be both seen and felt. Another suggestive point was the fact that the abdominal pulsation was altogether above the infra-costal line. It did not extend the entire length of the abdominal aorta. You can feel the thrill, but you do not feel a very positive tumor, which is evidently deep-seated, probably in the ciliac axis.

In the second case the pulsation is more evident and very visible. Here the tumor is much more evident, the thrill is

very intense, and there is a loud systolic and also a diastolic murmur. He has no bruit behind. His pains are not nearly so intense. The situation of the pulsation, its very wide area, the very pronounced character of the tumor, and its expansile pulsation, are features that make the diagnosis certain. One of the most important points in this case is its onset in early life; he is only 27, very early for aneurism.

The possibility is that lead, in which he worked for so many years, had caused the sclerosis of his arteries. In the first case the aneurism is probably in contact with the lower ribs on the left side. In this case I do not think the aorta has eroded the vertebræ to any great extent. He has not had the boring pains such as are almost always present when the aneurism is eroding the vertebræ.

We have had five instances of abdominal aneurism in the Hospital, out of a total of 57 aneurisms of the larger vessels. It is very much less common than aneurism of the thoracic aorta.

Some of you remember the man, Lee Kenny, who had a singularly movable tumor in the upper part of the abdomen, which was aneurismal, which pulsated with considerable force and which you could grasp in the hand. Dr. Halsted did a laparotomy, thinking it was possibly not in the aorta but in one of the branches, but it proved to be in the aorta. He was somewhat improved after the operation, but we lost sight of him.

In a certain number of aneurisms of the abdominal aorta a cure has been effected. The celebrated case of Murray was the first; the aneurism was seated low, just above the bifurcation, and digital compression for an hour caused cessation of pulsation in the sac, and patient lived for nine or ten years. The autopsy showed a healed aneurismal sac. There have been several other instances where compression either by fingers or the clamp cured the aneurism by filling the sac and securing consolidation.

In this first case I think operative procedures would be out of the question. In the second one the possibility of wiring has to be considered. In several cases this has been done successfully. In this man the operation would be justifiable.

Discussion of Dr. Pancoast's Diabetes in the Negro (*continued*).
See February Bulletin, p. 40.

Dr. Osler.—This case illustrates a point that was brought to my mind a few weeks ago. A woman with diabetes went to Europe in the middle of June. She had a slight cough at the time which had not attracted the attention of her physicians. In July the cough became worse, and her doctor in Ireland found extensive disease of one lung. On her return she refused to see her old physicians, as she blamed them for overlooking a serious condition of affairs and permitting her to go abroad. She persisted in this point, though I tried to explain that her trouble had developed very rapidly.

Here is a case in point. This man developed tuberculosis within a period of nine weeks and lost in weight from 180 to 130 pounds. The loss of weight and the rapid downward progress are well recognized features in some cases of diabetic phthisis.

NOTES ON NEW BOOKS.

Pathological Technique. A Practical Manual for the Bacteriological Laboratory. By Frank Barr Mallory, A. M., M. D., and James Homer Wright, A. M., M. D. (*W. B. Saunders, Philadelphia*, 1897.)

The manual which bears the above title comes to us from the pathological laboratories connected with the Harvard Medical School, and while it is offered as a practical guide for workers in pathological laboratories, we shall be much mistaken if it does not find a much wider sphere of usefulness. The volume, which is well made and of convenient size, is subdivided into three parts; the subject-matter of each, while closely connected with that of the other two, being treated in detail separately.

Part I, in which the technique of autopsies is outlined, contains a full and satisfactory presentation of the best recognized procedures in making post-mortem examinations. The authors have adhered to no one authority, but have chosen from several sources methods which they regard as the most useful and practical. While, as might naturally have been expected, the Virchow method is mainly followed, the authors have not felt themselves bound to follow it in all its details and do not hesitate to recommend the employment of certain procedures which have emanated from the Austrian school of pathologists. Many of the illustrations in this part of the work are borrowed from the little manual of Nauwerck, and the authors are to be commended for reproducing and making available for the English-speaking student these excellent drawings. In the part devoted to the section of the brain the method of Virchow is justly criticized as causing too much disturbance of the relations in the cortex, while that of Pitre, which is also given in detail, is not commended. In the light of our present knowledge the authors would seem to consider the hardening of the entire organ in formalin as affording the best means for future accurate study of the topography of focal lesions, while at the same time the tissue is preserved so as to be available for the finer histological methods. The demands of modern neurology, the growth of the knowledge of cerebral localization and the importance of following closely the various tracts have rendered it evident that the customary time which can be devoted to an autopsy is every day becoming more and more unsuitable for the examination and description of lesions in this organ.

On page 26 a typographical error has slipped into this part of the work. The statement that "The greenish discoloration seen earliest over the abdomen is due to *sulphats* of iron," is evidently intended to read, *sulphide* of iron.

Part II, which treats of the general methods of bacteriological examinations, is subdivided into (1) Bacteriological apparatus; (2) Culture media; (3) Bacteriological examinations at autopsies; (4) The methods of studying bacteria in cultures; (5) Bacteriological diagnosis; (6) Clinical bacteriology.

This section of the work is all that can be desired in a book of the scope of the present one. The directions for the preparations of media and cultures and the isolation of micro-organisms in pure culture and their identification, which is the ultimate purpose of bacteriological study, are clearly and succinctly stated. We fail, however, to notice any allusion to the autoclave for the sterilization of culture media. There is, in our opinion, no more valuable piece of apparatus for the bacteriological laboratory. Besides its other advantages it enables the time element in the preparation of such media to be greatly reduced. But, however convenient it may be to obviate the loss of time consumed in fractional sterilization, and whatever the advantages in having the media ready to use at once after their preparation, the chief value of the autoclave lies in the certainty with which, at a single exposure, even the most resistant spores (*e. g.* of the bacillus subtilis) are destroyed. The atmosphere of Boston or its climate may be unfavorable to the prevalence of epidemics of hay-bacillus infection, or perchance the city water

supply is free from contamination with this organism; but in the latitude of Baltimore, especially in the fall season, it constitutes a pest to the bacteriologist, against the ravages of which the autoclave alone has been found to furnish a sufficient protection. With the exception of blood serum we do not hesitate to put all culture media, including even gelatine (which is exposed for 6 or 8 minutes), through the autoclave at a pressure of two atmospheres and at a temperature approaching 120° C.

The routine examination by cultures and films or cover-slips is recommended in post-mortem examinations. We are glad to find this point emphasized. The day is perhaps not far distant when this procedure will be regarded as essential to the proper conduct of an autopsy, so that every examination will be deemed incomplete unless the bacteriological study has been carried out. Not a few problems in the causation of disease and of death have already received their solution through the systematic search for pathogenic bacteria in human post-mortem examinations. No modern physician, and still less a pathologist or bacteriologist, regards bacteria as the only living agents which cause the infectious diseases, and we are therefore bound to exercise due caution and a chariness in drawing conclusions based upon negative results from the bacteriological study in suspicious cases. It is not too much to hope that the near future will make amenable to cultivation and study the group of protozoa, just as the bacteria, by the introduction of solid culture media and the invention of a few simple mechanical processes, have been rendered so easy of observation. And when this feat shall have been accomplished, may not the whole group of exanthematous fevers be "resolved" and fall into their natural nosological places?

It is quite natural that differences of opinion should arise, especially regarding details, as to the best or most generally useful method to be employed in the systematic bacteriological study of autopsies. The authors of this manual advise as the best medium coagulated blood serum, which by their method of preparation is easily accessible for routine work. Of its suitableness as a culture medium there can be no question, but there remains the objection that where a mixture of bacterial forms or species prevails in the original material, their isolation can be most easily effected before the existing proportions are disturbed, and data of the relative numbers of each species present can be obtained only by an immediate separation. For this purpose the "plate" method, using preferably agar-agar, would seem to be the only one applicable. In the end, special cases will dictate special methods of procedure, and the rarity or frequency of departures from the rule will depend on circumstances, among which should perhaps be placed first the readiness with which the operator appreciates the unusual and his capacity to deal quickly with special problems as they arise. In carrying out a post-mortem examination in what is now regarded a proper manner, so many details have to be considered, that unless the time factor is to be entirely neglected, dexterity in operation and quickness in decision are faculties which are especially to be cultivated and by no means to be despised.

As regards the "time factor" the improvements in histological technique allow no free latitude. If the pathological histology of the future is to keep pace with its younger brother histology, and is to advance beyond the achievements of the period which ended with the semi-centennial just celebrated by Virchow's Archives, and which marks the era of the influence upon medical science of the cellular doctrine of organized nature, then minutes must replace hours in the time elapsing after death before autopsy in order that the organic tissues may be suitable for histological research.

The statement that the micro-organism causing actinomycosis has not as yet been proved to belong to the bacteria (fission-fungi) is made with due conservatism, but it seems hardly justifiable to place it provisionally among the cladothrices. If it is a bacterium it belongs, according to our present classification, among the streptothrices.

The differentiation of the smegma bacilli from the bacillus of tuberculosis is not quite so simple a matter as one little experienced in this undertaking might conclude from the remarks on pages 92 and 93. As the question is often an important one in diagnosis, it might not have been out of place to mention some of the difficulties and to have supplied other methods of distinction, especially the use of an alcoholic solution of methylene-blue, as recommended by Grethe.

Part III, which is devoted to the enumeration and description of histological and clinical microscopic methods, gives an excellent account of the processes employed in hardening, imbedding, sectioning, staining and mounting microscopic sections of tissues. The examination of sputa, blood, fæces, gastric contents and urine is also dealt with. Where so much is attempted it is not to be expected that all the headings will be treated of with equal completeness. The chief value of this chapter will be found in the pages devoted to histological methods, and it goes without saying that the special works dealing with clinical microscopy will need to be consulted by those who require more than a brief outline of matters relating to any one subject, for the minute details of which the authors could not spare space.

Drs. Mallory and Wright have given to the English-speaking student an excellent laboratory guide in the methods of modern pathological, histological and clinical study and research.

S. F.

BOOKS RECEIVED.

Twentieth Century Practice. An International Encyclopedia of Modern Medical Science, by Leading Authorities of Europe and America. Edited by Thomas L. Stedman, M. D. Vol. XIII. Infectious Diseases. 1898. 8vo. 621 pages. W. Wood & Co.

Biennial Report of the Department of Health of the City of Chicago, being for the Years 1895 *and* 1896. 1897. 8vo. 397 pages + 51 + 30. Press of Cameron, Amberg & Co., Chicago.

Case of Carcinoma of Descending Colon; Excision and Anastomosis; Recovery. By John H. Musser, M. D., and Thomas S. K. Morton, M. D. Reprinted from the University Medical Magazine, July, 1896.

Angina Pectoris: Its Relation to Dilatation of the Heart. By John H. Musser, M. D. Reprinted from the American Journal of the Medical Sciences, September, 1897.

A Case of Lucæmia. By John H. Musser, M. D., and Joseph Sailer, M. D. Reprinted from the Transactions of the Association of American Physicians, 1896.

On the Disappearance of Endocardial Murmurs of Organic Origin. By John H. Musser, M. D. Reprinted from the British Medical Journal, October 16, 1897.

A Clinical Study of Widal's Serum Diagnosis of Typhoid Fever. By John H. Musser, M. D., and John M. Swan, M. D. Reprinted from the Journal of the American Medical Association, August 14, 1897.

A Text-Book of the Diseases of Women. By Henry J. Garrigues, A. M., M. D. Second Edition. Thoroughly Revised. 1897. 8vo. 728 pages. W. B. Saunders, Philadelphia.

Elements of Latin. For Students of Medicine and Pharmacy. By George D. Crothers, A. M., M. D., and Hiram H. Bice, A. M. 1898. 12mo. 242 pages. The F. A. Davis Co., Philadelphia.

ERRATA—JANUARY BULLETIN.

In footnote, page 12, read 1629 instead of 1829.

In footnotes on page 13, the references to Vanderwiel and Schurig should be reversed.

On page 16, line 12, the word nasal should be inserted before reflex neuroses.

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GENERAL STATEMENT.

The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital.

The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter.

Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry, and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, beside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

The Annual Announcement and Catalogue will be sent upon application. Inquiries should be addressed to the

REGISTRAR OF THE JOHNS HOPKINS MEDICAL SCHOOL, BALTIMORE.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by THE FRIEDENWALD CO., Baltimore. Single copies may be procured from Messrs. CUSHING & CO. and the BALTIMORE NEWS COMPANY, Baltimore. Subscriptions, $1.00 a year, may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for fifteen cents each.